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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/187,661	11/05/98	SHIRLEY	B 5784-3

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Intellectual Property - R440
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EXAMINER	
MOEZIE,F	
ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 05/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/187,661	Shirley et al
Examiner	**Art Unit**
F. MOEZIE	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *11/17/00 and 3/13/01*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-7, 9-11, and 13-44* is/are pending in the application.

4a) Of the above, claim(s) *5-7, 9-11, 14, and 15* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, 4, 13, 16-20, and 28-44* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1, 3-7, 9-11, and 13-44* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3 1/2*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

STATUS OF CLAIMS

Claims 1, 3, 4, 13, 16-20 (amended) and new 28-44 (not designated new) are pending prosecution in this Office action.

Claims 2, 8 and 11have been canceled (11/17/00). Claims 5-12, 14, 15, and 21-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper received July 12, 1999

The earlier Restriction Requirement is made **Final**.

Cancellation of the nonelected claims is advised.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3, 4, 13, 18-20 and 28-44 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The critical buffer pH which imparts stability to the formulation and is essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure (specification, page 5, lines 15+). See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Note, regardless of the method of preparing the claimed highly concentrated IGF-I formulations, i.e., manipulation of the pH or the use of the solubilizing agent,

it is critical that the pH of the buffer in the syrup formulation be the same in the resulting formulations (e g., specification - page 5, line 5+). See, also Fig. 1 and Examples 1-3.

In claims 1 and the claims dependent thereon, the terminology "biologically active variants thereof' render the claims indefinite as to the structure of the variants being claimed. Incorporation of the subject matter of claim 28 into claim 21 will overcome this ground of rejection.

The following terminologies: "low, less than, greater than, at least" in claims 1, 13, 34, 42 are relative terms and renders the claims indefinite. The cited terminologies have not been defined in the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For these reasons the claims are vague and indefinite regarding their metes and bounds.

Claims 1, 3, 4, 13, 16-20 and 28-42 are indefinite regarding the lack of the critical pH of the buffer in the formulation. Furthermore, the term "mg/ml" (designating a solution volume) does not find basis in the claims because a term such as "an aqueous" prior to "formulation" is missing from the claims.

Claim 13 is an improper kit claim. Claim is drawn to one formulation. See page 2, lines 2+ and page 12, lines 14+, for guidance.

Claims 16, 38, 40 and 43 are duplicative of claims 1, 34, 40 and 42, respectively. The intended use for a formulation does not distinguish one formulation over another.

REJECTION - 35 U.S.C. 103 (a)

Claims 1, 3, 4, 13, 16-20, 28-38 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al., in US Patent No.5,410,026.

Chang et al teach that: the solubility of the isolated insoluble IGF-I is increased using a single buffer containing a chaotropic agent. See, the paragraph bridging column 26-27. Moreover, at column 10, the typical pH range for the buffer and the chaotropic agents suitable for increasing the solubility of and IGF-I or an analogue thereof in solution are also taught. Hence, the reference clearly shows that the use of guanidinium-containing compounds enhance the solubility of IGF-I at higher pH (pH of typically at least 7.5), thereby providing for a stable IGF-I composition having higher concentrations. See the entire document.

It would have been obvious to an ordinary art skilled at the time the invention was made to use the conditions cited by the reference for obtaining a formulation of IGF-I or analogues thereof with higher concentration of the active agent(s) therein - as claimed. To choose a particular concentration range (mg/ml) is well within the skill of an ordinary art skilled and greatly depends on the intended use for the resulting formulation.

Claims 39-41 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Chang et al and Johnson et al in Nature Medicine, 7/1996.

The teachings of Chang et al have been disclosed above. However, Chang et al., do not teach the incorporation of their product in PLGA microsphers. Applicant admits that IGF-I syrup could be used to encapsulate IGF-I in PLGA according to Johnson et al., page 20, lines 3+ One of ordinary skill in the art would have been motivated to make the PLGA containing product for its long lasting effects.

RESPONSE TO REMARKS

The Response filed March 13, 2001, regarding the nonresponsive action (mailed January 31, 2001) has been considered and found persuasive. Hence, the elected invention claims, as indicated above, are examined on their merits in this Office action.

Applicant's Remarks filed November 17, 2000 have been fully considered and found persuasive in-part.

Regarding the request for a copy of the earlier PTO Form 1449 and the Supplemental PTO Form 1449, a second copy of the Forms are attached to this Office action for Applicants' records

The earlier rejection of the claims under 35 U.S.C. 112, first paragraph, regarding the lack of enablement and description, as applied earlier, is withdrawn in view of the amendments and remarks.

The rejection of the claims under 112, second paragraph, is maintained for the reasons cited above. The relative terms would have to be deleted or defined in the claims to overcome the indefiniteness.

The earlier rejection of the claims under 35 U.S.C. 103 (a) over the teachings of Johnson et al is withdrawn in view of the applicants' remake.

CONCLUSION

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to F.T. Moezie at telephone number (703) 305-4508.

F.T. MOEZIE, Ph.D.
PRIMARY EXAMINER
ART UNIT 1653